Femtosecond diffraction imaging and coded aperture holography of a single cell

Sebastien Boutet[1,2,3], Michael J. Bogan[3], Joanna Lee[4], Stefano Marchesini[4], Anton Barty[3], Matthias Frank[3], Saša Bajt[3], Bruce Woods[3], Joshua W. Shaevitz[4], Daniel A. Fletcher[4], Marvin Seibert[2], Filipe Maia[2], Florian Burmeister[2], Erik Marklund[2], Janos Hajdu[1,2], Henry N. Chapman[2,5]

[1]Stanford Linear Accelerator Center, [2]Laboratory of Molecular Biophysics, Department of Cell and Molecular Biology, Uppsala University, [3]University of California, Lawrence Livermore National Laboratory, [4]University of California, Berkeley, [5]Center for Biophotonics Science and Technology, University of California, Davis

The fourth generation light sources or free electron lasers possess many unique characteristics which promise to lead to interesting developments in the field of diffractive imaging of biological samples. Above all else, the greatly increased brilliance of these new sources compared to third generation sources appears most attractive. However, in itself, the increased intensity of the beam produced by FEL sources does not help eliminate the main limiting factor for imaging of biological material, namely the damage caused to the sample by the beam. The problem is indeed magnified for FEL sources as the damage occurs even faster. Only when combined with extreme short pulse duration (on the order of 100 femtoseconds or less) does the increased brilliance become an asset for biological imaging. The radiation damage to the sample can be circumvented by simply having all the x-rays in the beam interact with the object of interest in a period of time shorter than the time required for the damage to occur. We will present the first experimental demonstration of this flash imaging technique on a whole biological cell. While a single femtosecond x-ray pulse scattering from a single cell deposited on a membrane completely destroyed the sample, our results show that a two dimensional diffraction pattern could be measured and phase retrieval algorithms used to reconstruct an undamaged density of the cell to within the measured resolution. This technique could prove, at least in two dimensions, to be a powerful tool to study the structure of cells at near atomic resolution when shorter wavelength FELs become available.

Some of the inherent difficulties with iterative phase retrieval techniques such as the occasional lack of convergence and the difficulty to determine when the solution has been found can be overcome by using known reference objects, i.e. using holographic references. Using a single small pinhole as a reference object allows for high resolution structure determination but leads to a small signal level. A clever choice of a complex reference object can preserve the high resolution while boosting the holographic signal dramatically. We will present results from single FEL shot coded aperture holography of a single biological cell and discuss how such a technique at fourth generation sources can beat radiation damage while avoiding computationally intensive phase retrieval object reconstruction.